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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/500,397	02/08/2000	Gerald Soff	4228-1-1-1	2549

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Laura A Coruzzi
Pennie & Edmonds LLP
1155 Avenue of the Americas
New York, NY 10036-2711

EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/500,397	SOFF ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-21,23,24 and 76-90* is/are pending in the application.

4a) Of the above claim(s) *78 and 87* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-21, 23-24, 76-77, 79-86, 88-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's election with traverse the invention of hemangiomas in paper of 08/24/04 is acknowledged and entered.

The traverse is on the ground that inventions 1-20 are neither independent nor distinct. Applicant argues that inventions 1-20 relate to methods that share the same objective, i.e. increase the amount of angiostatin in vivo, and criteria for success, i.e. inhibit blood vessel formation.

Applicant argues that in the alternative, the invention hemangiomas should be examined together with the invention ocular angiogenic diseases, because the search only require 8 specific angiogenic diseases, and it would not be a serious burden for the Examiner to search all the groups together.

Applicant's arguments have been considered but are found not to be persuasive.

Inventions 1-20 are distinct, because the methods of inventions 1-20 have different objectives, dosages/and or schedules used, response variables, criteria for success. It is noted that the inventions 1-20 are drawn to a method for treating different angiogenic diseases, and not a method for increasing the amount of angiostatin in vivo in a single angiogenic disease. Thus the methods of inventions 1-20 have different objectives, i.e. treating different angiogenic diseases, which have different characteristics and properties. Similarly, the methods of inventions 1-20 require different

dosages and criteria for success, i.e. different angiogenic diseases are successfully treated, because different angiogenic diseases have different characteristics and properties. Moreover, the responses of different angiogenic diseases to plasminogen activator would be variable, because they are different diseases with different properties and characteristics, and because not all different diseases have the same response to a drug.

Different searches would be required for different angiogenic diseases, because not all different diseases have the same response to a drug, and since the search for different methods would not be co-extensive, it would be a serious burden for the Examiner to search all the groups together.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 19-21, 23-24, 76-77, 79-86, 88-90, a method for treating angiogenic disease, in particular hemangiomas, are being examined. Claims 78, 87 are withdrawn from consideration as being drawn to non-elected inventions.

The following are the remaining rejections.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Rejection under 35 USC 112, first paragraph of claims 19-21, 23-24, 76-77, 79-86, 88-90, pertaining to lack of enablement for a method for treating angiogenic disease, in particular hemangiomas, remains for reasons already of record in paper of 08/18/03.

Applicant argues that Berman is irrelevant to enablement of the method of the invention because Berman does not use the claimed protocol -- i.e., Berman does not administer a "therapeutically effective amount'" of plasminogen activator that increases the amount of angiostatin in the animal. Applicant argues that instead Berman injects 20 ul aliquots of urokinase (3.7 CTA Units) intrastromally into the comeas of 2 to 3.5 kg rabbits. Applicant argues that in contrast, Applicants claim the administration of an amount of plasminogen activator effective to increase the amount of angiostatin in the animal to treat the angiogenic disease.

Applicant argues that by contrast to the protocol used by Berman, when plasminogen activator is administered in accordance with the claimed methods of the present invention, the amount of angiostatin generated in vivo will increase and thereby inhibit angiogenesis. Applicant argues that moreover, Applicants have demonstrated that angiostatin inhibits angiogenesis in comeas (see Gately et al., 1996, Cancer Res. 56: 4887-90, at Fig. 3 and its accompanying discussion at p. 4889, col. 1, last paragraph).

Applicant again refers to the prosecution of the parent application SN= 08/991,761, which claims a method for treating cancer, using a plasminogen activator.

Applicant's arguments set forth in paper of 08/24/04 have been considered but are not deemed to be persuasive for the following reasons:

Applicant has not taught that plaminogen activator is effective in treating any angiogenic diseases, and in particular hemangiomas. Applicant has not taught which amount of plasminogen activator does not promote vascularization, an opposite effect of

angiostatin, nor which amount of plasminogen activator would be effective for cancelling the effect of vascularization, nor which amount of plasminogen activator would produce an adequate amount of angiostatin effective for treating any angiogenic diseases, in particular hemangiomas, in the presence of the vascularization effect by the plasminogen activator per se. Treating angiogenic diseases, including hemangiomas, using a plasminogen activator, however is unpredictable, in view of the teaching of Berman et al (of record) that a plasminogen activator, urokinase, actually promotes vascularization of the cornea in vivo, which has an opposite effect of angiostatin.

Further, although angiostatin per se inhibits angiogenesis in cornea, the claims are not drawn to a method for treating angiogenic diseases, using angiostatin per se, or a method for inhibiting angiogenesis in cornea, using angiostatin per se. In view of the above teaching in the art that plaminogen activator induces vascularization in the cornea in vivo, an opposite effect of angiostatin, one cannot predict that the claimed method using a plasminogen activator would be effective in treating any angiogenic diseases, including hemangiomas.

Further, although a very small amount of angiostatin is detected in cancer patients, one cannot predict that patients with any angiogenic diseases, including hemangiomas, would produce angiostatin when treated with urokinase, because different diseases have different characteristics, and properties, and that response to a drug is not the same in different diseases.

Further, even if angiostatin is produced in patients with any angiogenic diseases, including hemangiomas, it is unpredictable that the effect of angiostatin produced in

patients with angiogenic diseases would be adequate, and/or would not be masked or encountered by the vascularization effect of the plasminogen activator, such urokinase, supra, especially in view that the level of angiostatin detected in plasma of cancer patients treated with urokinase is barely noticeable.

Moreover, it is unpredictable that one can adjust the level of plasminogen activator to generate an effective dosage of angiostatin, because plasminogen activator also has vascularization effect. Applicant has not taught which amount of plasminogen activator would produce more angiostatin than vascularization in any angiogenic diseases, including hemangiomas. Applicant has not taught which level of angiostatin is adequate, in the presence of vascularization, for treating any angiogenic diseases, including hemangiomas.

Concerning Applicant's referring to Application SN 08/991761, Applicant is reminded that each case is decided on its own facts.

It is well settled that whether similar claims have been allowed to others is immaterial. See In re Giolito, 530 F.2d 397, 188 USPQ 645 (CCPA 1976) and Ex parte Balzarini 21 USPQ2d 1892, 1897 (BPAI 1991).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS

September 27, 2004

SUSAN UNGAR, PH.D
PRIMARY EXAMINER